



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re the Application of:) Group Art Unit: 1644

MARRACK et al.) Examiner: Ewoldt, G.

Serial No.: 09/844,928)

Filed: April 26, 2001)

Atty. File No.: 2879-76)

For: "PRODUCT AND PROCESS FOR
REGULATION OF T CELL
RESPONSES")

DECLARATION OF
YOSEF REFAELI
(under 37 CFR 1.132)

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Yosef Refaeli, declare as follows:

1. I am an expert in the field of immunology and I am the first-named author of Refaeli et al., "Biochemical Mechanisms of IL-2-Regulated Fas-Mediated T Cell Apoptosis", *Immunity* 8:615-623 (1998).

2. This Declaration under 37 CFR 1.132 is being submitted in conjunction with a Response to an Office Action having a mailing date of June 17, 2005.

3. I am familiar with the disclosure of the above-identified patent application and I have reviewed the currently pending claims. In addition, I have reviewed the Examiner's rejection of Claims 1-3, 9, 14-15 and 52 under 35 U.S.C. § 103 in the June 17 Office Action. Finally, I have reviewed the reference by Lenardo that is cited in this same rejection (Lenardo, "Interleukin-2 Programs Mouse $\alpha\beta$ T Lymphocytes for Apoptosis", *Nature* 353:858-861 (1991)).

4. My comments in paragraph 5 below are directed to the Examiner's position that it would be obvious to combine IL-15, to stimulate memory T cell production, with anti-IL-2, to remove IL-2 and reduce T cell activation-induced cell death (AICD), allowing for the maximal production of memory T cells. In particular, my comments are directed to the Examiner's citation of Lenardo and Refaeli et al. to support the rejection. The Examiner states that Lenardo teach that

IL-2 is required for the programmed cell death of mature (antigen-activated) T cells and that cells that escape IL-2-induced apoptosis may become memory cells. In addition, Refaeli et al. is cited for expanding the teachings of Lenardo and concluding that IL-2 is involved in T cell homeostasis.

5. Although I agree that Lenardo's publication and my own publication (Refaeli et al.) teach that IL-2 enhances AICD of mature, activated T lymphocytes, it is my opinion that one of skill in the art can not say, based on the teachings of either Lenardo or Refaeli et al., that T cells that are affected by AICD are related to memory T cells. Therefore, one also can not assume, based on these publications, that if mature T lymphocytes are protected from AICD, they will become memory T cells. Such an assumption would be complete speculation, since there are no data provided in either of Lenardo's publication or my own publication to support such a hypothesis. Neither publication evaluates the effect of IL-2 or the inhibition of IL-2 on T cells of a memory phenotype. Therefore, I disagree with the Examiner's position that Lenardo teach that T cells that escape AICD become memory T cells, or that my own publication somehow supports this hypothesis, since neither publication provides any evidence that this statement is correct. Accordingly, it does not appear to me to be obvious that inhibition of IL-2 will stimulate memory T cells.

6. I hereby declare that all statements made herein of my own are true and that all statements made on information and belief are believed to be true; and further that the statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the subject application or any patent issuing therefrom.

11/17/05

Date

Yosef Refaeli

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